19. A composition according to claim 1, 2 or 17, wherein said substrate is a fiber optic bundle.

20. A method according to claim 6 or 7 wherein said substrate is selected from the group consisting of glass or plastic.

21. A method according to claim 6 or 7, wherein said substrate is a fiber optic bundle.--.

### REMARKS

Claims 1-7 and 15-21 are pending. For the Examiners convenience a copy of the currently pending claims is appended hereto. Support for the amendment of claims 2-5 and 15 is found in the claims as filed. Support for claim 17 is found in claim 2 as filed. Support for claims 18-21 is found at p. 9, lines 10-17.

### RESPONSE TO REJECTIONS

# Rejection Under 35 U.S.C. § 112.

Currently pending claims 1-7 and 15-16 are rejected under 35 U.S.C. § 112, first paragraph for lack of written description. Basically the Office Action suggests that the "limitation of discrete or individual sites on the substrate for microsphere attachment is separate from random distribution of microspheres." The Examiner points to p. 9, line 30 to p. 10, line 17 as support for the assertion that "patterning of sites ... is an alternative to a random distribution and not practiced at the same time." Applicants respectfully traverse.

Although Applicants agree that p. 9, line 30 to p. 10 line 17 indicates that the substrate may contain patterned sites or alternatively it may contain random distribution of sites, this section in no way describes that manner in which microspheres are distributed on the surface. That is, the specification is describing that the sites on the surface of the substrate may be agranged in a pattern or may be random. As noted by the Examiner, at p. 10, line 7, the "sites may be a pattern...or randomly distributed."

However, as noted in the previous Response to Office Action, the specification is replete with disclosure related to the random distribution of microspheres on a patterned substrate. As indicated at p. 6, lines 30-31, "[t]he beads may be randomly distributed on the array". At p. 6, lines 19-20 is noted that "beads, also termed microspheres, ...are distributed on a substrate comprising a patterned surface of discrete sites". At. p. 6, lines 26-27 is noted that "the beads are randomly distributed on a patterned surface."

Accordingly, in contrast the Examiner's assertion that inclusion of the term "random" in the claims constitutes new matter, Applicants submit that the specification fully supports the claims as currently pending. As noted above, the specification clearly describes that microspheres may be randomly distributed on a patterned surface. Accordingly, Applicants respectfully request the Examiner to withdraw this rejection.

# Rejections Under 35 U.S.C. § 102(b) and (e)

Currently pending claims 1-7 and 15-16 stand rejected under 35 U.S.C. § 102(b) and (e) as being anticipated by Ekins et al. (U.S.P.N. 5,516,635). It is acknowledged that the Examiner has maintained and reiterated the rejection from the previous office action; the rejection is maintained in part "due to anticipation of removal of the ... NEW MATTER". Applicants respectfully traverse the rejection.

Initially, Applicants assert for the reasons described above, that the claims as pending contain no new matter. That is, the specification fully supports claims directed to microspheres randomly distributed on a surface. Accordingly, the claims have not been amended to remove this language.

As such, Applicants submit that Ekins fails to teach random distribution of microspheres on a surface comprising discrete sites. In fact, Ekins teaches the opposite, that microspheres are targeted to particular locations by an antibody attached to the bead. That is, the capture binding agent, which is spotted on the substrate, defines the site to which the beads attach. Accordingly, Applicants submit that Ekins fails to anticipate any of the present claims.

Moreover. Applicants submit that Ekins fails to teach microspheres comprising a bioactive agent and an identifier binding ligand that will bind a decoder binding ligand such that the identification of the bioactive agent can be elucidated. That is, as the Examiner noted, Ekins teaches a microsphere with a label and an antibody. The Examiner indicates that the antibody is a bioactive agent. The Examiner also indicates that the "different markers such as multiple fluorescent labels decode target binding as an identifier."

However, Applicants respectfully remind the Examiner that the claimed invention (of claim 1, and those that depend from claim 1) includes "an identifier binding ligand that will bind a decoder binding ligand such that the identification of the bioactive agent can be elucidated". To this end, Applicants note that the marker of Ekins fails to bind a decoder binding ligand. Moreover, the marker of Ekins does not allow for the identification of the bioactive agent to be elucidated. That is, the marker of Ekins merely allows for identification of the presence of a microsphere; it does not identify the bioactive agent on the microsphere. Accordingly, Applicants submit that the microspheres of Ekins contain only a single bioactive agent and a label for the detection of the bead.

As to the Examiner's rejection of claim 2, Applicants respectfully note that Ekins fails to teach that microspheres are randomly distributed on the substrate. Accordingly, Applicants submit that Ekins fails to anticipate claim 2 and those claims that depend from claim 2.

Likewise, as to the rejection of claims 6 and 7, Applicants submit that Ekins fails to teach random distribution of microspheres on a substrate. Moreover, Ekins fails to teach that microspheres comprise a bioactive agent and an identifier binding ligand that will bind at least one decoder binding ligand such that the identification of the bioactive agent can be elucidated.

Accordingly, Applicants submit that Ekins fails to anticipate any of the presently pending claims. Applicants respectfully request withdrawal of the rejections.

### CONCLUSION

Applicants submit that the claims as amended are in form for immediate allowance and

the Examiner is respectfully requested to early notification to that effect. The Examiner is invited to contact the undersigned at (415) 781-1989 if any issues may be resolved in that manner.

Respectfully submitted,
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Dated: \_\_\_\_\_

# APPENDIX- CURRENTLY PENDING CLAIMS

1. An array composition comprising:

a) a substrate with a surface comprising discrete sites; and

b) a population of microspheres comprising at least a first and a second subpopulation,

wherein each subpopulation comprises:

i) a bioactive agent; and

ii) an identifier binding ligand that will bind a decoder binding ligand such that

the identification of the bioactive agent can be elucidated;

wherein said microspheres are randomly distributed on said surface.

2. An array composition comprising:

a) a substrate with a surface comprising discrete sites; and

b) a population of microspheres comprising at least a first and a second subpopulation,

wherein each subpopulation comprises a bioactive agent and does not comprise an

optical signature, wherein said microspheres are randomly distributed on said surface.

3. (Amended) A composition according to claim 1 [or 2], 2 or 17, further comprising at least

one decoder binding ligand.

4. (Amended) A composition according to claim 1 [or 2], 2 or 17, wherein said bioactive agents

are nucleic acids.

5. (Amended) A composition according to claim 1 [or 2], 2 or 17, wherein said bioactive agents

are proteins.

6. A method of making a composition comprising:

7

- a) forming a surface comprising individual sites on a substrate;
- b) randomly distributing microspheres on said surface such that said individual sites contain microspheres, wherein said microspheres comprise at least a first and a second subpopulation each comprising a bioactive agent and do not comprise an optical signature.
- 7. A method of making a composition comprising:
  - a) forming a surface comprising individual sites on a substrate;
  - b) randomly distributing microspheres on said surface such that said individual sites contain microspheres, wherein said microspheres comprise at least a first and a second subpopulations each comprising:
    - i) a bioactive agent; and
    - ii) an identifier binding ligand that will bind at least one decoder binding ligand such that the identification of the bioactive agent can be elucidated.
- 15. (Amended) The composition according to claim 1 [or claim 2] <u>2 or 17</u>, wherein said discrete sites are wells.
- 16. (Amended) The method according to claim 6[,] or claim 7, [claim 8, claim 13 or claim 14,] wherein said discrete sites are wells.--.

Please add the following new claims:

- -17. An array composition comprising:
  - a) a substrate with a surface comprising discrete sites; and
  - b) a population of microspheres comprising at least a first and a second subpopulation, wherein each subpopulation comprises a bioactive agent and does not comprise a label, wherein said microspheres are randomly distributed on said surface.

- 18. A composition according to claim 1, 2, or 17, wherein said substrate is selected from the group consisting of glass and plastic.
- 19. A composition according to claim 1, 2 or 17, wherein said substrate is a fiber optic bundle.
- 20. A method according to claim 6 or 7 wherein said substrate is selected from the group consisting of glass or plastic.
- 21. A method according to claim 6 or 7, wherein said substrate is a fiber optic bundle.--.